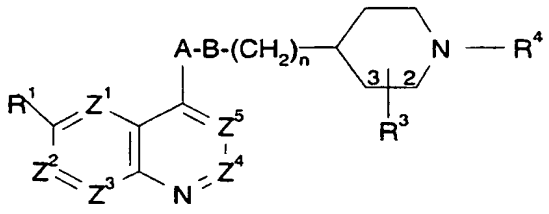
Claims

1. A method of treatment of bacterial infections in mammals, which method comprises the administration to a mammal in need of such treatment of an effective amount of a compound of formula (I) or a pharmaceutically acceptable derivative thereof:



(I)

wherein:

one of Z^1, Z^2, Z^3, Z^4 and Z^5 is N or CR^{1a} and the remainder are CH;

R^1 is selected from hydroxy; (C_{1-6}) alkoxy optionally substituted by (C_{1-6})alkoxy, amino, piperidyl, guanidino or amidino optionally N-substituted by one or two (C_{1-6})alkyl, acyl or (C_{1-6})alkylsulphonyl groups, NH_2CO, hydroxy, thiol, (C_{1-6})alkylthio, heterocyclylthio, heterocyclyloxy, arylthio, aryloxy, acylthio, acyloxy or (C_{1-6})alkylsulphonyloxy; (C_{1-6})alkoxy-substituted (C_{1-6})alkyl; halogen; (C_{1-6})alkyl; (C_{1-6})alkylthio; trifluoromethyl; nitro; azido; acyl; acyloxy; acylthio; (C_{1-6})alkylsulphonyl; (C_{1-6})alkylsulphoxide; arylsulphonyl; arylsulphoxide or an amino, piperidyl, guanidino or amidino group optionally N-substituted by one or two (C_{1-6})alkyl, acyl or (C_{1-6})alkylsulphonyl groups, or when one of Z^1, Z^2, Z^3, Z^4 and Z^5 is N, R^1 may instead be hydrogen;

R^{1a} is selected from hydrogen and the groups listed above for R^1;

R^3 is in the 2- or 3-position and is:
carboxy; (C_{1-6})alkoxycarbonyl; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, aminocarbonyl(C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylsulphonyl, trifluoromethylsulphonyl, (C_{1-6})alkenylsulphonyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl or (C_{2-6})alkenylcarbonyl and optionally further substituted by (C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, aminocarbonyl(C_{1-6})alkyl or (C_{2-6})alkenyl; cyano; tetrazolyl; 2-oxo-oxazolidinyl optionally substituted by R^{10}; 3-hydroxy-3-cyclobutene-1,2-dione-4-yl; 2,4-

thiazolidinedione-5-yl; tetrazol-5-ylaminocarbonyl; 1,2,4-triazol-5-yl optionally substituted by R^{10}; or 5-oxo-1,2,4-oxadiazol-3-yl; or

R^3 is in the 2- or 3-position and is (C_{1-4})alkyl or ethenyl substituted with any of the groups listed above for R^3 and 0 to 2 groups R^{12} independently selected from:

thiol; halogen; (C_{1-6})alkylthio; trifluoromethyl; azido; (C_{1-6})alkoxycarbonyl; (C_{1-6})alkylcarbonyl; (C_{2-6})alkenyloxycarbonyl; (C_{2-6})alkenylcarbonyl; hydroxy optionally substituted by (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl, (C_{2-6})alkenylcarbonyl or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylcarbonyl or (C_{2-6})alkenylcarbonyl; amino optionally mono- or disubstituted by (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl, (C_{2-6})alkenylcarbonyl, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylsulphonyl, (C_{2-6})alkenylsulphonyl or aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl; aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, aminocarbonyl(C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl or (C_{2-6})alkenylcarbonyl and optionally further substituted by (C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, aminocarbonyl(C_{1-6})alkyl or (C_{2-6})alkenyl; oxo; (C_{1-6})alkylsulphonyl; (C_{2-6})alkenylsulphonyl; or (C_{1-6})aminosulphonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl;

provided that when R^3 is disubstituted with hydroxy or amino and carboxy containing substituents these may optionally together form a cyclic ester or amide linkage, respectively;

and provided that R^3 is other than (C_{1-4})alkyl or ethenyl substituted by (C_{1-6})alkoxycarbonyl or aminocarbonyl optionally substituted by (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl or (C_{2-6})alkenylcarbonyl and optionally further substituted by (C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, aminocarbonyl(C_{1-6})alkyl or (C_{2-6})alkenyl and 0 to 2 groups R^{12};

wherein R^{10} is selected from (C_{1-4})alkyl; (C_{2-4})alkenyl; aryl; a group R^{12} as defined above; carboxy; aminocarbonyl wherein the amino group is optionally substituted by hydroxy, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{1-6})alkylsulphonyl, trifluoromethylsulphonyl, (C_{1-6})alkenylsulphonyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{2-6})alkenyloxycarbonyl or (C_{2-6})alkenylcarbonyl and optionally further substituted by (C_{1-6})alkyl or (C_{2-6})alkenyl; cyano; or tetrazolyl;

R^4 is a group $-CH_2-R^5$ in which R^5 is selected from:

(C_{3-12})alkyl; hydroxy(C_{3-12})alkyl; (C_{1-12})alkoxy(C_{3-12})alkyl; (C_{1-12})alkanoyloxy(C_{3-12})alkyl; (C_{3-6})cycloalkyl(C_{3-12})alkyl; hydroxy-, (C_{1-12})alkoxy- or (C_{1-12})alkanoyloxy-(C_{3-6})cycloalkyl(C_{3-12})alkyl; cyano(C_{3-12})alkyl; (C_{2-12})alkenyl; (C_{2-12})alkynyl; tetrahydrofuryl; mono- or di-(C_{1-12})alkylamino(C_{3-12})alkyl; acylamino(C_{3-12})alkyl; (C_{1-12})alkyl- or acyl-aminocarbonyl(C_{3-12})alkyl; mono- or di-(C_{1-12})alkylamino(hydroxy) (C_{3-12})alkyl; optionally substituted phenyl(C_{1-2})alkyl, phenoxy(C_{1-2})alkyl or phenyl(hydroxy)(C_{1-2})alkyl; optionally substituted diphenyl(C_{1-2})alkyl; optionally substituted phenyl(C_{2-3})alkenyl; optionally substituted benzoyl or benzoylmethyl; optionally substituted heteroaryl(C_{1-2})alkyl;and optionally substituted heteroaroyl or heteroaroylmethyl;

n is 0, 1 or 2;

either A-B is NHC(O)NH or NHC(O)O, or

A is NR^{11}, O, $S(O)_x$ or CR^6R^7 and B is NR^{11}, O, $S(O)_x$ or CR^8R^9 where x is 0, 1 or 2 and wherein:
each of R^6 and R^7 R^8 and R^9 is independently selected from: H; thiol; (C_{1-6})alkylthio; halo; trifluoromethyl; azido; (C_{1-6})alkyl; (C_{2-6})alkenyl; (C_{1-6})alkoxycarbonyl; (C_{1-6})alkylcarbonyl; (C_{2-6})alkenyloxycarbonyl; (C_{2-6})alkenylcarbonyl; hydroxy, amino or aminocarbonyl optionally substituted as for corresponding substituents in R^3; (C_{1-6})alkylsulphonyl; (C_{2-6})alkenylsulphonyl; or (C_{1-6})aminosulphonyl wherein the amino group is optionally substituted by (C_{1-6})alkyl or (C_{1-6})alkenyl;
or R^6 and R^8 together represent a bond and R^7 and R^9 are as above defined;
or R^6 and R^8 together represent –O- and R^7 and R^9 are both hydrogen;
or R^6 and R^7 or R^8 and R^9 together represent oxo;
and each R^{11} is independently H, trifluoromethyl, (C_{1-6})alkyl, (C_{1-6})alkenyl, (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, aminocarbonyl wherein the amino group is optionally substituted by (C_{1-6})alkoxycarbonyl, (C_{1-6})alkylcarbonyl, (C_{1-6})alkenyloxycarbonyl, (C_{2-6})alkenylcarbonyl, (C_{1-6})alkyl or (C_{1-6})alkenyl and optionally further substituted by (C_{1-6})alkyl or (C_{1-6})alkenyl;

provided that A and B cannot both be selected from NR^{11}, O and $S(O)_x$ and when one of A and B is CO the other is not CO, O or $S(O)_x$.

2. A compound of formula (IA) or a pharmaceutically acceptable derivative thereof which is a compound of formula (I) as defined in claim 1 wherein R^3 is other than (C_{1-6})alkoxycarbonyl; optionally substituted aminocarbonyl, CN or COOH.

3. A compound according to claim 2 wherein Z^5 is CH or N and Z^1-Z^4 are each CH.

4. A compound according to claim 2 or 3 wherein R^1 is methoxy, amino- or guanidino-(C_{3-5})alkyloxy, guanidino(C_{3-5})alkyloxy, piperidyl(C_{3-5})alkyloxy, nitro or fluoro, and R^{1a} is hydrogen.

5. A compound according to any of claims 2 to 4 wherein R^3 is in the 3-position and is CH_2CO_2H or 2-oxo-oxazolidinyl.

6. A compound according to any of claims 2 to 5 wherein $AB(CH_2)_n$ is $(CH_2)_3$.

7. A compound according to any of claims 2 to 6 wherein R^4 is (C_{5-10})alkyl, unsubstituted phenyl(C_{2-3})alkyl or unsubstituted phenyl(C_{3-4})alkenyl.

8. A compound of formula (I) as defined in claim 1 selected from:

[3R, 4R]-1-Heptyl-3-(1-(R or S)-hydroxy-2-cyanoethyl)-4-[3-(6-methoxyquinolin-4-yl)propyl]piperidine;

[3R, 4R]-1-Heptyl-3-(2-(R or S)-oxo-oxazolidin-5-yl)-4-[3-(6-methoxyquinolin-4-yl) propyl] piperidine;

[3R, 4R]-1-Heptyl-3-(2-cyanoethyl)-4-[3-(6-methoxyquinolin-4-yl) propyl] piperidine;

[3R, 4R]-1-Heptyl-3-(3-carboxyethyl)-4-[3-(6-methoxyquinolin-4-yl) propyl] piperidine;

[3R, 4R]-1-Heptyl-3-carboxy-4-[3-(6-methoxyquinolin-4-yl) propyl] piperidine;

[3R, 4R]-1-Heptyl-3-(carboxymethyl)-4-[3-(6-methoxyquinolin-4-yl) propyl] piperidine;

[3R, 4R]-1-Heptyl-3-(1-(R or S)-hydroxy-2-carboxyethyl)-4-[3-(6-methoxyquinolin-4-yl)propyl]piperidine;

[3R, 4R]-1-Heptyl-3-(2-(*E*-)-carboxyethenyl)-4-[3-(6-methoxyquinolin-4-yl)propyl]piperidine;

N-(cis-3-(R/S)-Ethoxycarbonyl-1-heptyl-4-(S/R)-piperidyl)-N'-(6-methoxyquinolin-4-yl)urea;

N-(cis-3-(R/S)-Ethoxycarbonyl-1-heptyl-4-(S/R)-piperidyl)-N'-(6-methoxy-[1,5]-naphthyridin-4-yl)urea;

N-(cis-3-(R/S)-Aminocarbonyl-1-heptyl-4-(S/R)-piperidyl)-N'-(6-methoxy-[1,5]-naphthyridin-4-yl)urea;

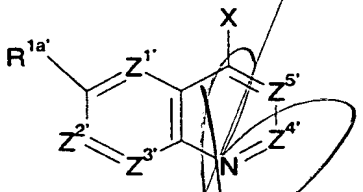
[3R, 4R]-1-Heptyl-4-[3-(R/S)-hydroxy-3-(6-methoxyquinolin-4-yl)propyl]-3-(2-(R or S)-oxo-oxazolidin-5-yl)-piperidine;

[3R, 4R]-1-Heptyl-3-cyanomethyl-4-[3-(R/S)-hydroxy-3-(6-methoxyquinolin-4-yl)propyl]piperidine;

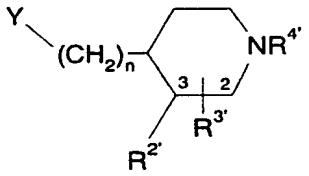
[3R, 4R]-1-Heptyl-3-cyanomethyl-4-(2-(R)-hydroxy-3-(6-methoxyquinolin-4-yl)propyl]piperidine;
N-(cis-3-(R/S)-Carboxy-1-heptyl-4-(S/R)-piperidyl)-N'-(6-methoxyquinolin-4-yl)urea;
cis-3-(R/S)-Ethoxycarbonyl-1-heptyl-4-(S/R)-(6-methoxyquinolin-4-yl)aminocarbonyl-oxypiperidine;
cis-3-(R/S)-Carboxy-1-heptyl-4-(S/R)-(6-methoxyquinolin-4-yl)aminocarbonyl-oxypiperidine;
a compound 18-36 from Table 1;
or a pharmaceutically acceptable derivative of any of the foregoing compounds.

9. A process for preparing compounds of formula (IA) as defined in claim 2, or a pharmaceutically acceptable derivative thereof, which process comprises:

(a) reacting a compound of formula (IV) with a compound of formula (V):



(IV)



(V)

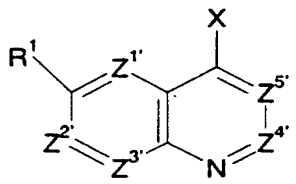
wherein Z^1, Z^2, Z^3, Z^4 and Z^5, m, n, R^1, R^2, R^3 and R^4 are as defined in formula (I), and X and Y may be the following combinations:

(i) X is M and Y is $CH_2CO_2R^x$
(ii) X is CO_2R^y and Y is $CH_2CO_2R^x$
(iii) one of X and Y is $CH=SPh_2$ and the other is CHO
(iv) X is CH_3 and Y is CHO
(v) X is CH_3 and Y is CO_2R^x
(vi) X is $CH_2CO_2R^y$ and Y is CO_2R^x
(vii) X is $CH=PR^z_3$ and Y is CHO
(viii) X is CHO and Y is $CH=PR^z_3$
(ix) X is halogen and Y is $CH=CH_2$
(x) one of X and Y is COW and the other is $NHR^{11'}$ or NCO
(xi) one of X and Y is $(CH_2)_p$-V and the other is $(CH_2)_qNHR^{11'}$, $(CH_2)_qOH$, $(CH_2)_qSH$ or $(CH_2)_qSCOR^x$ where p+q=1
(xii) one of X and Y is CHO and the other is $NHR^{11'}$
(xiii) one of X and Y is OH and the other is $-CH=N_2$

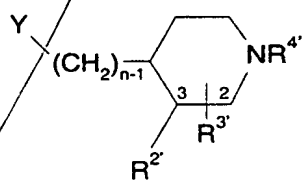
in which V and W are leaving groups, R^x and R^y are (C_{1-6})alkyl and R^z is aryl or (C_{1-6})alkyl, or

(xiv) X is NCO, Y is OH or NH_2 ;

(b) reacting a compound of formula (IV) with a compound of formula (Vb):



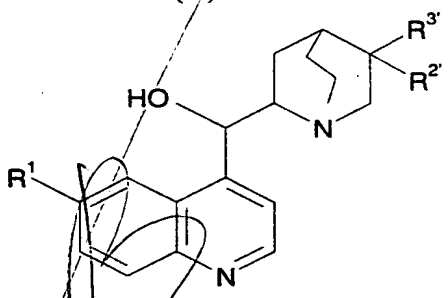
(IV)



(Vb)

wherein Z^1, Z^2, Z^3, Z^4 and Z^5, m, n, R^1, R^2, R^3 and R^4 are as defined in formula (I), X is $CH_2NHR^{11'}$ and Y is CHO or COW or X is CH_2OH and Y is $-CH=N_2$;

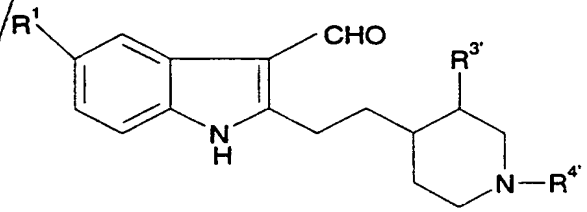
(c) rearranging a compound of formula (II):



(II)

to give a compound of formula (III) which is a compound of formula (I) where Z^1-Z^5 are CH, n is 1, A-B is $COCH_2$ and R^2 is H, or a compound of formula (VII) which is a compound of formula (I) where n is 1, A-B is $CHOHCH_2$ or CH_2CHOH and R^2 is H; or

(d) photooxygenating a compound of formula (VI):



(VI)

in which $Z^{1'}$-$Z^{5'}$ are Z^1-Z^5 or groups convertible thereto, $R^{11'}$, $R^{1'}$, $R^{2'}$, $R^{3'}$ and $R^{4'}$ are R^{11}, R^1, R^2, R^3 and R^4 or groups convertible thereto, and thereafter optionally or as

necessary converting $R^{11'}$, $R^{1'}$, $R^{2'}$, $R^{3'}$ and $R^{4'}$ to $R^{11'}$, R^1, R^2, R^3 and R^4, converting $Z^{1'}$-$Z^{5'}$ to Z^1-Z^5, converting A-B to other A-B, interconverting R^{11}, R^1, R^2, R^3 and/or R^4 and forming a pharmaceutically acceptable derivative thereof.

10. A pharmaceutical composition comprising a compound of formula (IA) as defined in claim 2, or a pharmaceutically acceptable derivative thereof, and a pharmaceutically acceptable carrier.

11. The use of a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable derivative thereof in the manufacture of a medicament for use in the treatment of bacterial infections in mammals.

12. A pharmaceutical composition for use in the treatment of bacterial infections in mammals comprising a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable derivative thereof, and a pharmaceutically acceptable carrier.